Dairy cattle genomics: Tools to accelerate genetic improvement?[1]

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ABSTRACT: Traditional selection based on genetic merit calculated from phenotypic and pedigree information has been tremendously effective at improving production in dairy cattle. Hypothetically, genetic improvement could be accelerated even further for yield and other economically important traits by directly selecting upon the genetic differences underlying the phenotypes. To elucidate these genetic differences, research strategies based on genomic science have been developed to identify economic trait loci (ETL). Once resolved with respect to position in the genome, DNA marker-based tests that identify ETL can be practically applied to enhance selection in a commercial setting. To date, most dairy-related ETL have been detected in Holstein grandsire families using the granddaughter design. Because the marker intervals identifying these ETL are not resolved well enough for accurate selection in current populations, ETL analyses have been or are being extended to include ancestral animals that connect family pedigrees and current generations of nonprogeny-tested animals from within the founder animal pedigree. Increasing genotypic and phenotypic information in this manner alleviates two statistical limitations often associated with ETL interval refinement in experimental populations. First, population size is no longer limited or biased by previous selection. In addition, the inheritance of ETL can be traced from historic families of interest to current generations relevant to the industry. After allele frequency and contribution to phenotype are determined in current populations, those ETL most beneficial for the industry can be accurately used for selection. As an aid to ETL mapping in dairy cattle, efforts have been initiated to catalog as many bovine genes as possible by generating expressed sequence tags (EST) from cDNA clones. These clones represent gene expression at the mRNA level in various tissue types present in cattle. Mapping EST with sequence identity to human genes onto the bovine genetic map is improving the comparative map between species and will aid future investigations in determining genes that underlie ETL. Furthermore, cDNA microarrays constructed with the aid of EST data can be used for hybridization analysis to characterize gene-expression patterns and identify genetic pathways important for animal production and udder health.

Key Words: Dairy Cattle, Genetic Markers, Genomic Analysis

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Introduction

For more than 40 yr, dairy breeders have used genetic evaluations to identify superior animals. Selective use of these animals improved phenotypic measures for milk production and milk components, especially in Holstein cattle. However, there are some limitations to selecting on predicted breeding values. Most breeding schemes do not account for population effects on genetic diversity, and selection is optimized for genetic response in the next generation rather than the highest long-term response (Meuwissen, 1997). This selection approach also has limited ability to improve lowly heritable traits without adversely affecting production. Lowly heritable traits often include those associated with disease resistance, reproduction, duration of productive life, and some conformation traits correlated with fitness. Information from genetic markers that identify desirable alleles of economically important traits could be used with breeding values to guide mating decisions, resulting in genetic gains over a broader range of traits. In addition, marker-assisted selection (**MAS**) could be used to select the most desirable phenotypes affected by nonadditive gene action or epistatic interactions between loci. Soller and Beckmann (1983) proposed that MAS can also reduce the costs the AI industry incurs using progeny test evaluations as the sole method for screening candidate bulls.

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Before MAS can be applied in commercial dairying, economic trait loci (**ETL**) must be identified, validated, and characterized for utility in improving genetic gain. Thus, this article is a review of the processes of ETL mapping in dairy cattle using a comprehensive genomics-based approach. The discussion is focused on current investigations to develop reliable MAS schemes and to identify the causative genetic variation underlying production and type traits in Holsteins. An example of how this strategy has been used to investigate a putative ETL for dairy form is included.

Economic Trait Loci Identification

Development of commercially viable MAS systems begins with the identification of genetic variation associated with segregating ETL. The basic resources critical to successfully performing ETL identification across the entire cattle genome are 1) resource populations with relatively accurate phenotypic records and accompanying genomic DNA samples, 2) polymorphic DNA markers that have been positioned throughout the genome, 3) laboratory capacity to perform high-throughput genetic analysis of marker samples, and 4) ETL detection algorithms for genetic analysis of genotypic and phenotypic data.

Dairy Resource Populations

The statistical power and accuracy of ETL detection are dependent upon population size, pedigree structure, and the measurable phenotypic differences within a pedigree. Many livestock populations currently used to map ETL were developed following an F_2 or backcross design using founder animals that had large phenotypic differences. This approach has been successfully used to identify numerous ETL in a variety of livestock species. In the case of dairy cattle, the dominance of the Holstein breed in North America has limited the utility of a crossbred ETL mapping population. However, ETL detection in Holsteins can be successfully performed using an alternative approach. Weller and colleagues (1990) proposed the use of the granddaughter design (**GDD**) as a method for ETL detection in dairy cattle made possible by the existence of large half-sib sire families created by extensive use of AI. This design relies on finding a significant statistical association between allele inheritance patterns for a marker locus and the standard deviation of phenotypic means for a measured trait (Figure 1). The phenotypic means are determined by dividing granddaughters into two groups based on transmission of marker alleles from the grandsire to son (sire of granddaughter). An advantage of GDD over the comparable F_2 design is that for a specific power of ETL detection fewer animals need to be analyzed with DNA markers.

The Dairy Bull DNA Repository (**DBDR**) is an example of one experimental GDD population established for mapping ETL in large U.S. Holstein grandsire families (Da et al., 1994). This population consists of over 1,500 sires from 35 grandsire families with > 40 sons. The DNA was made available for each animal through semen contributed by several United States dairy AI organizations. The 35 grandsires represent trait data for over 500,000 granddaughters used to calculate genetic evaluations by USDA, The National Association of Animal Breeders, and Holstein Association USA. The genetic evaluations determine predicted transmitting abilities (**PTA**) and daughter yield deviations (**DYD**) for the different production and conformation traits recorded by the dairy industry (Van Raden and Wiggans, 1991). Most of the DBDR sires were popular in late 1980s and are no longer widely used in breeding programs.

Because the DBDR population is static and considered historic, a new population was created to bridge the gap in pedigree and molecular genetic information between the historic families of the DBDR and current generations in production. These animals were made available through the Cooperative Dairy DNA Repository (**CDDR**), which is an ongoing collection that includes all breeds of dairy cattle (Ashwell et al., 2000). This collection was designed to receive semen for young bulls as they enter progeny testing. A major advantage of ETL mapping in the CDDR is that population size is not limited or biased by progeny test results, and these characteristics help alleviate the limitations of ETL interval refinement inherent in the DBDR. Currently, eight of the largest North American studs are contributing semen for DNA extraction. To date, a total of 63 families with over 25 sons are contained within the 6,576 animals already contributed to the collection. Genetic information generated from the CDDR will allow more accurate determinations of allele frequency and estimates of ETL contribution to phenotype. Together, this information will help determine those ETL most beneficial for the industry that can be accurately used for selection.

Dairy-related ETL mapping projects have also been initiated in New Zealand, France, and Brazil. The resource populations in these studies will utilize an F_2 population design to detect ETL. Similarly, U.S. producers could benefit from development of a Jersey-Holstein F_2 population for ETL mapping with the recent changes in the milk payment orders that pay premiums based on protein yield. Construction of an F_2 dairy population is a large undertaking because of long generation times and the expense of generating sufficient daughters for production phenotypes. However, there are significant advantages of such a design that include the ability to record important phenotypes not typically available (e.g., temperament, feed conversion, and milking speed), the ability to evaluate the production value of crossbreeding as an alternative to purebred dairy cattle, and providing a research herd for evaluation of Holstein-Jersey cross cattle as this breeding scheme increases in popularity among commercial dairy producers.

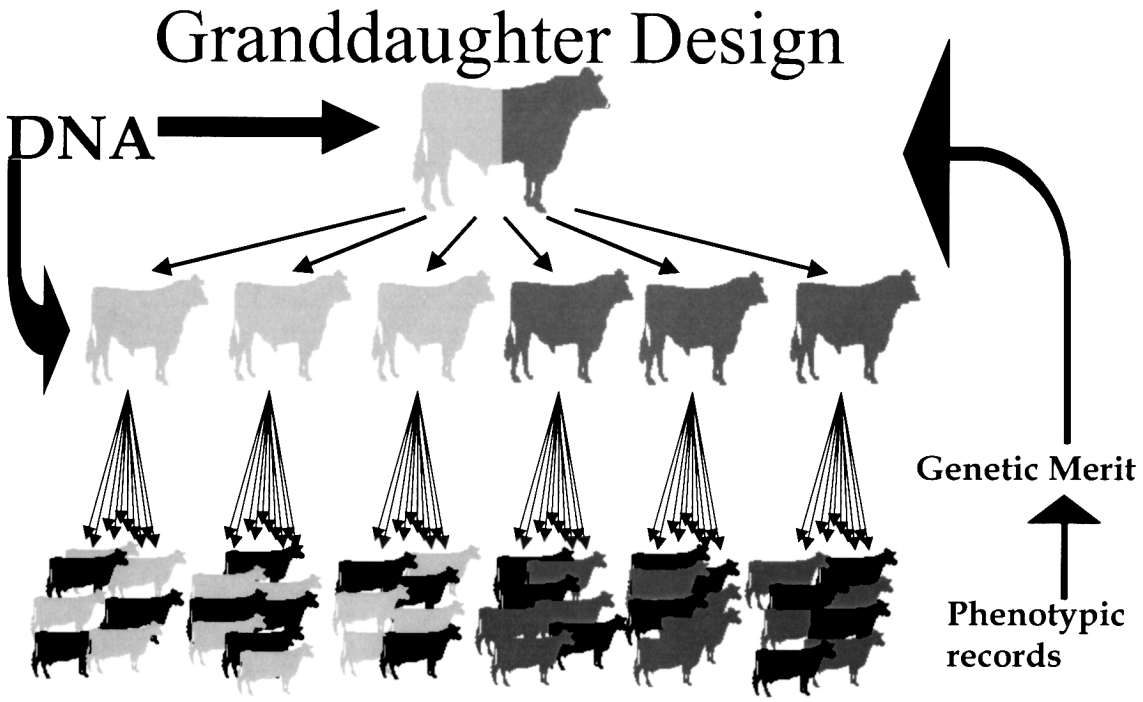

Figure 1. Depiction of the granddaughter design population used to map economic trait loci (ETL) in dairy cattle, where large half-sib families were created by extensive use of AI with semen from high genetic merit sires. The silhouette of the grandsire (top) is shaded with two colors to represent allele heterozygosity at a marker locus. Sons (middle), also characterized by genotyping, are placed in either of two groups depending upon the allele inherited. The genetic merit estimates generated from daughter information (bottom) for each group are then used to perform marker association tests. A significant difference in the phenotypic mean between each allele group of sons signifies the detection of potential ETL.

Bovine DNA Markers

One prerequisite to identifying ETL is a genetic map with sufficient informative markers to maximize genome coverage. Because meioses and marker heterozygosity may limit map development and resolution of an ETL, a high density of informative markers on a reference linkage map ensures flexibility in selection of markers for genomic scans in experimental populations. The majority of genetic markers on current bovine maps (Barendse et al., 1997; Kappes et al., 1997) are microsatellites (Weber and May, 1989). Combined, these reference linkage maps denote the approximate genomic positions of over 1,800 unique markers.

Detection of ETL in the DBDR families requires heterozygous grandsire marker genotypes. Microstallite markers remain the best resource for performing genome-wide ETL detection experiments in populations of low-genetic diversity like the Holstein breed due to availability, known reference map position, and relatively high heterozygosity indices. A typical approach to performing a genome scan would involve selecting markers placed across the entire bovine genome (3,000 cM) at 20 cM intervals with high heterozygosity indices (60 to 80%). Web sites containing reference linkage maps, like that available from the USDA Meat Animal Research Center, contain additional information related to ease of scoring genotypes and PCR amplification characteristics (http://sol.marc.usda.gov/genome/cattle). This information aids in the selection of the most useful markers for any given location in the genome. Following these criteria for primary marker selection is not always completely effective due to the lower levels of genetic diversity in Holsteins. For example, markers selected by this method had an average heterozygosity of 50 to 60% in the DBDR population (Van Tassell et al., 2000), which was approximately 10% below that observed in crossbreed animals used to generate the USDA reference linkage map (Kappes et al., 1997). The lowered marker heterozygosity often creates gaps in genome coverage larger than 20 cM, thereby reducing ETL detection power for these genomic regions. These gaps can sometimes be removed by selecting additional markers from the reference linkage map.

High-Throughput Genotyping

A major bottleneck in performing any genome-wide scan is generating the thousands of marker genotypes necessary for detecting significant marker effects. The need for high throughput genotyping has required researchers to continually improve the methodologies used to generate marker genotypes. Issues commonly dealt with include 1) efficient sample preparation (i.e.,

PCR multiplexing of markers), 2) accurate sample analysis (i.e., genotype scoring), and 3) well-organized data management. Automation of these three processes requires an investment in time, money, and technical expertise. Early strategies for high-throughput genotyping were labor-intensive, and marker genotypes had to be scored manually. Identification of ETL of the eight largest DBDR sire families required several years of genotyping before a genome-wide analysis could be performed (Ashwell et al., unpublished data). Recent advances in instrumentation for liquid handling robotics, thermal cyclers, automated DNA analyzers, and genotyping software have reduced the labor and time requirements necessary to process the necessary marker genotypes for a genome-wide analysis. The most common bovine markers used to generate genetic data, microsatellite markers, are not always easily amenable to newer genotyping instrumentation. For example, most bovine microsatellite markers were developed for generating genotypes using oil immersion PCR reactions, radiolabeled nucleotides or primers, and denaturing acrylamide gels. Because of this, most of the markers were designed to produce relatively small allele amplimers (100 to 200 bps). Some reoptimization (i.e., determine optimal annealing temperature, redesign primers) of microsatellite markers is necessary to allow maximum compatibility with automated DNA analyzers. This also includes developing informative marker multiplexes to reduce cost and time of analysis. Additionally, no large sets of commercially optimized markers are available for performing a genome-wide analysis for ETL as there are for human studies (Applied Biosystems, Foster City, CA). As an example of a high-throughput genotyping facility for cattle, our laboratory is equipped with nine 384-well PTC-200 thermal cyclers (MJ Research Inc., Watertown, MA), one RSP-100 robotic liquid handler (Tecan, Research Triangle Park, NC), and one ABI-3700 automated DNA analyzer (Applied Biosystems, Foster City, CA). This equipment provides the capacity to process over 20,000 multiplexed marker reactions on a weekly basis.

In the near future, alternative high-throughput genotyping platforms that are based on the detection of single nucleotide polymorphisms (**SNP**) will be available. Instruments designed for detection of SNP should reduce the time, labor, and cost to produce a marker genotype. The USDA expressed sequence tag (**EST**) project is developing SNP marker resources for ETL mapping in resource populations. Currently, genomic DNA amplimers generated from the MARC reference sires are being sequenced to identify gene intron-associated SNP. The primers used to produce these DNA amplimers were designed by software that aligns human genomic and bovine EST sequence to find introns. Introns are targeted for SNP discovery, because the frequency of identifying polymorphisms is higher than that found in coding sequence. These gene-associated SNP are used to map EST to the reference linkage map (T.P.L. Smith, personal communication). At this time, there are not enough highly informative SNP markers available to identify ETL on a genome-wide basis. Because SNP are biallelic markers, a much larger set of markers will be needed to produce the informative haplotype information needed for genome analysis.

Marker-Trait Analyses and Economic Trait Loci Detection

A variety of statistical methods have been utilized to detect dairy-related ETL using the GDD population structure (for a partial summary, see http://spinal.tag.csiro.au/cgi-bin/cgdqt). There are two common approaches for ETL detection. Marker-trait association analysis can be performed by either methods for ANOVA or by determining identity by descent. The second method, marker regression or interval analysis, requires genotypic data from several markers to estimate ETL location relative to the known positions of markers within the chromosome linkage group (Haley and Knott, 1992). However, no consensus approach has been established as to how data should be analyzed and what significance thresholds should be used to detect and report ETL. For example, the DBDR has been used extensively by two groups of researchers to identify ETL associations with PTA and DYD for the different production and conformation traits. Heyen et al. (1999) have successfully completed a genome-wide scan of eight grandsire families for seven production and health traits (DYD). In this study, genotypes generated from 174 microsatellite markers provided 85% coverage of the entire genome, and marker effects ($P < 0.01$) were detected by joint analysis across families on 11 chromosomes. The critical threshold values of significance were determined using formulas developed by Lander and Kruglyak (1995). As a result, only the marker effects that exceeded suggestive and genome-wide significance levels were those identified for fat percentage on chromosomes 3 and 14, respectively.

In contrast, Ashwell and colleagues (1996) initiated marker association studies to identify ETL affecting somatic cell score in the seven largest families of the DBDR. Within-family analysis was performed using ANOVA as a simple approach for comparing marker genotypes at a single locus to DYD. This project was later expanded to identify additional ETL affecting 38 traits including traits for milk production, calving difficulty, conformation, and canonical traits on a genome-wide basis in eight DBDR families (Van Tassell et al., 2000). The thousand of test statistics produced from this expanded analysis made the significance threshold of $P < 0.01$ inadequate for detecting Type I errors (false-positives). In this study, subsequent test results were screened for errors using the permutation test described by Churchill and Doerge (1994) to calculate trait-wise significance values. Recently, a genome-wide analysis was performed using marker genotypes for 155 microsatellite markers, and marker effects across families that exceeded experiment-wise critical thresh-

old values ($P < 0.1$) were detected for 29 production and type ETL on 13 chromosomes (Ashwell et al., unpublished data).

Several other genome-wide scans to detect dairy-related ETL were performed on GDD resource populations, and a variety of different statistical analysis methods were used to detect marker-trait associations (Georges et al., 1995; Zhang et al., 1998; Schrooten et al., 2000). These investigations have identified unique and similar putative ETL for production traits, which is not surprising considering the pedigree connections between popular Holstein sire families. Comparing results across all studies would suggest that ETL affecting milk production traits are segregating on chromosomes 3, 6, 14, and 20. These ETL need further characterization and localization on the genetic map before accurate selection can be applied to current populations.

Fine Mapping Economic Trait Loci for Marker-Assisted Selection

A relatively fast and inexpensive method for improving the map resolution of ETL is to saturate the area with markers (for review see Georges, 1999). Some refinement can be achieved by generating genotypes from additional markers that according to the reference linkage maps should be near potential ETL, but resolution can be limited by the varied availability of informative markers across the genome. New informative markers are often required to further resolve ETL. These markers can be generated in a region-specific manner either by developing MS markers from chromosome-specific DNA libraries (Sonstegard et al., 1997b) or by comparative mapping (Sonstegard et al. 1997a).

Effective population size also affects ETL resolution. Additional refinement can be obtained by identifying animals in which a recombination event has taken place between a nearby flanking marker and the putative ETL. This requires extending ETL analyses to include ancestral animals that connect family pedigrees and current generations of animals in the pedigree, thereby increasing the chances of detecting an informative recombination event. Expanded pedigree analysis also can provide better estimates of ETL allele frequency and contribution to phenotype. Generally, refinement of ETL to a narrow genetic interval (< 5 cM) defined by several flanking markers should justify subsequent studies to validate and better characterize ETL for MAS in extant populations.

An Example of Fine Mapping for a Dairy Form Economic Trait Loci

An ETL of significant interest was detected on bovine chromosome 27 (**BTA27**), where strong evidence for an association between BM203 marker genotypes and dairy form ETL ($P = 0.000021$) was detected in a single grandsire family (Ashwell et al., 1998). Dairy form is defined as a conformation trait based upon body conditioning and has a moderate relationship with milk production (Holstein Association USA, 1999). In dairy cattle, a cow's proficiency to store adequate fat and then utilize these depots appropriately during lactation is genetically correlated with productive life and incidence of metabolic disease (Rogers et al., 1999). Selection for more extreme dairy form may increase the incidence of some metabolic diseases. In the case of the dairy form ETL, flanking markers could be used to select animals with decreased probability for metabolic disease without adversely affecting milk production, if no marker effects for milk production traits were detected on BTA27. The apparent relationship between dairy form and animal health makes this an attractive ETL for validation, further characterization, and possibly MAS application.

Before extensive research effort was focused on the dairy form ETL, the results of the initial marker association test for BM203 (Ashwell et al., 1998) had to be confirmed. The experimental strategy was to generate genotypic data from all available markers from the BTA27 reference linkage map and to determine by interval analysis estimates of intrachromosomal location for dairy form effects and the magnitude of allelic difference in DBDR family 8 (Van Tassell et al., 1998). BTA27-specific microsatellite markers (n = 21) were tested for heterozygosity in DBDR grandsire 8, but only 11 were useful for further analysis. A total of 12 marker genotypes generated from family 8 were analyzed assuming additive gene effects. These results revealed a significant ETL effect for dairy form localized to the telomeric region, and no significant effects on milk production traits were detected (Van Tassell et al., unpublished data). Heyen et al. (2000) also confirmed the existence of a dairy form ETL on BTA27 in a separate study.

Additional evidence for ETL can be obtained by comparing detection results across populations. In the case of the dairy form ETL on BTA27, a genome wide analysis of the USDA/MARC F1 bull resource population (Casas et al., 1998) revealed ETL for marbling with nominally significant effects close to the telomere (Casas et al, 2000). Individuals inheriting a Belgian Blue allele had more intramuscular fat than those inheriting a MARC III composite allele. This ETL is related to that for dairy form, in that both are associated with fat deposition.

The combined information generated from fine mapping experiments on BTA27 provided strong evidence for ETL related to fat deposition. Even if the ETL between studies are unrelated at the DNA sequence level, further characterization of this region of the genome is justified.

Complex Pedigree Analysis

Additional characteristics of the dairy form ETL identified in DBDR family 8 need to be determined before

implementing MAS. These include developing new markers flanking the ETL, identifying the statistical limits of ETL map resolution, determining allele frequencies in selection populations, and characterizing inheritance patterns for this region of the genome between resource and selection populations. Aside from developing new markers, these characteristics are being determined by expanding ETL analysis of dairy form into current generations of family 8 pedigrees found in the CDDR population (Sonstegard et al., unpublished data). The initial analysis of family 8 consisted of 79 sons, and the complex pedigree analysis will include over 800 sons and grandsons. In addition, DNA from the great-grandsire and half-sibs of the grandsire will be analyzed to provide more information on the effects of founder alleles. An ETL analysis of this pedigree design requires a more sophisticated approach to analysis that accounts for the genetic relationship between animals. The analysis algorithm developed by Thallman et al. (2001a,b) provides the statistical components needed to determine inheritance patterns, predict genotyping errors, and estimate founder allele effects from complex pedigrees. This rigorous analysis coupled with the increase in genetic data from the extended pedigree should yield ETL results (< 5cM) that allow for reliable and accurate implementation of MAS at AI organizations.

Finding the "Gene"

If MAS schemes for commercial use are the applied research goals of ETL mapping in dairy cattle, then identifying and characterizing the biological effects of the causative genetic variation are the more basic research goals. Successful identification of the "genes" underlying ETL provides not only the most accurate markers for selection, but also identifies critical biochemical pathways for further investigation and manipulation. The most common experimental strategy undertaken to initiate positional cloning of ETL is the identification of positional candidate genes by comparative mapping. As stated earlier, comparative mapping also represents a potentially efficient way to fine map through the development of new informative markers near ETL. The process of comparative mapping is based on the overall conservation of synteny between species, which allows information from the gene-rich human map to be applied to low-resolution gene map of cattle. Positional candidate genes for new marker development and mapping can only be properly selected after identification of conserved syntenic segments, establishment of the boundaries of conservation, and evaluation of gene-order changes within the candidate segment. Initial comparative maps between humans and cattle were primarily based on somatic cell panel studies, which did not clearly establish boundaries of conserved synteny across the entire genome.

Comparative Map of BTA27

To generate more informative markers near the dairy form and marbling ETL, construction of a BTA27 comparative map was initiated. Fourteen genes were selected for mapping based on previously identified regions of conservation between the cattle and human genomes (http://bos.cvm.tamu.edu/htmls/Bov27.html). Markers were developed from the bovine orthologs of genes found on human chromosome 1, 4, 8, and 14. Seven of these 14 gene markers mapped to BTA27 (Sonstegard et al., 2000). Five of these seven markers were estimated to be within 15 cM of the telomere, and genotypes from DBDR family 8 have already been added to our analyses of dairy form ETL (Sonstegard et al., unpublished data). Map information generated from the other seven genes not syntenic with BTA27 refined the breakpoint locations of conserved segments between species and revealed three areas of disagreement with the previous comparative map (Figure 2). Comparative map alignment based on these results strongly suggested the conserved segment orthologous to HSA8p21-q11 contains ETL for lipid metabolism in cattle. Unfortunately, none of the genes that have been functionally characterized and mapped to this region of the human genome would seem to meet subjective criteria as positional and functional candidate genes for lipid metabolism ETL in cattle.

Improving the Comparative Map

New markers developed through comparative map information have successfully aided the identification of genes that underlie traits with large phenotypic effects (Kambadur et al., 1997; Cockett et al., 1999). However, this approach was also severely limited by the low resolution of previous bovine gene maps. Mapping projects to improve access to human sequence and gene maps are ongoing.

Recently, Band and colleagues (2000) developed a radiation hybrid map that positioned 768 genes with identity to human orthologs. This comparative map suggests there is a minimum of 105 conserved segments of genome between the two species. This genomic tool will be valuable for targeted mapping of ETL-containing regions.

Another project complementary to improving the comparative map is the USDA bovine EST project. The overall goals of this project were to catalog nearly every bovine gene, and then map those genes that would provide comparative coverage between the entire bovine and human genomes. To date, over 157,000 bovine EST have been published in the dbEST database of GenBank with over 100,000 of these being submitted by USDA. Mapping of SNP of over 1,000 of these EST onto the USDA linkage map is nearing completion (T.P.L. Smith, personal communication). Upon completion of this comparative linkage map, positional candidate genes will be easily identified for ETL associated with

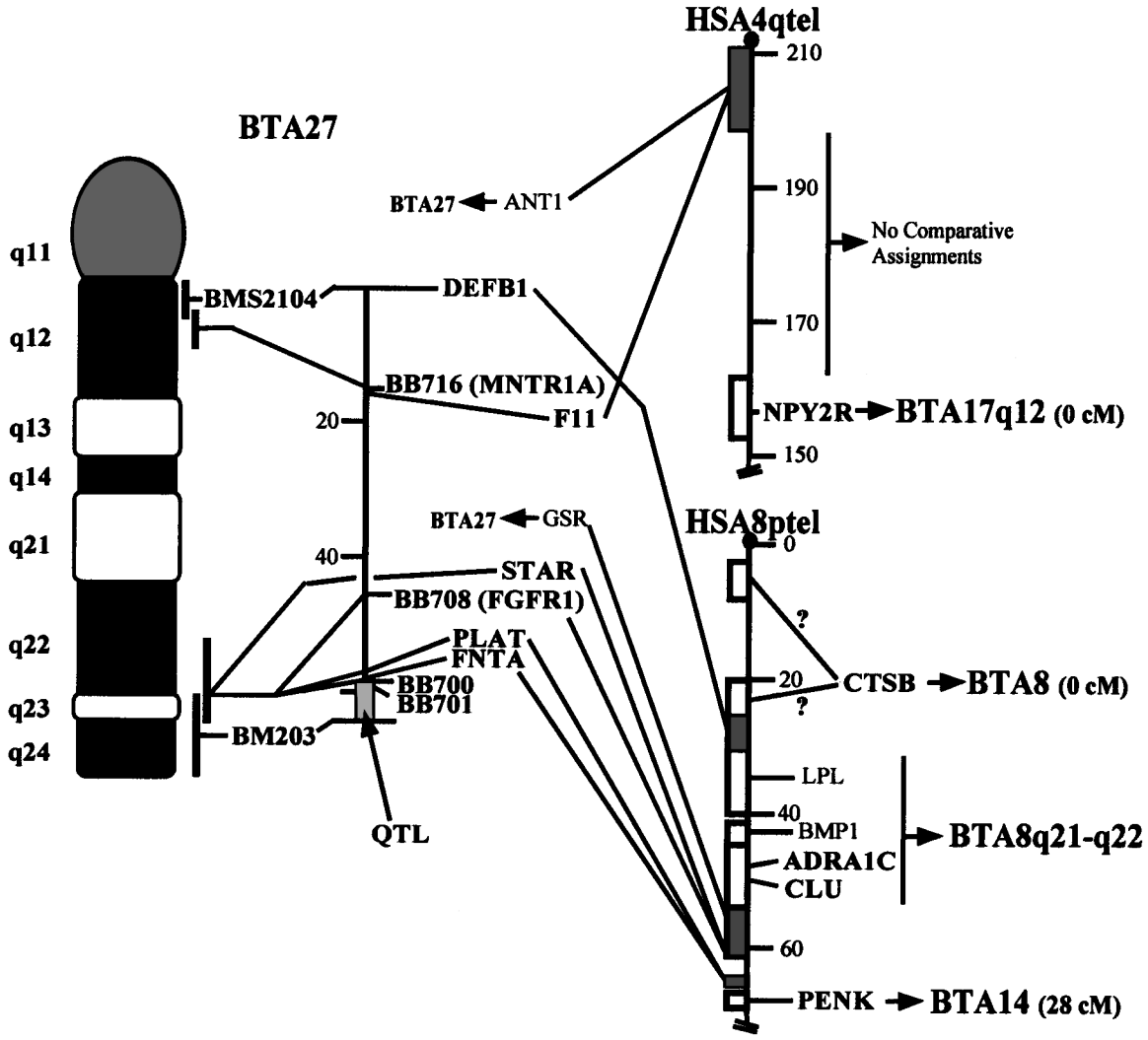

Figure 2. Comparative alignment of bovine chromosome 27 (BTA27) comprehensive map (left) and partial transcript maps of human chromosome 48 (HSA4q) and HSA8p (right). Thick vertical bars next to ideogram of a G-banded BTA27 indicate positions of physical map assignments. Integration to BTA27 linkage map and alignment with the human maps are indicated by solid and dashed lines between maps and gene symbols. Estimated positions for bovine and human loci are given in cM. Gray-filled box on bovine linkage map represents approximate positions of QTL for marbling and dairy form. Genetic intervals containing human loci are represented by boxes attached to axis of transcript map, and these interval bins were derived from the GB4 series radiation hybrid maps (http://www.ncbi.nlm.nih.gov/genemap99/page.cgi?F=Home.html). Filled boxes represent segments of human genome potentially conserved on BTA27. "?" denotes a positional discrepancy for the assignments of CTSB to HSA8p.

any marker throughout the entire genome. This process will be automated and made available through a relational database (Keele et al., 1994), so no actual map development is necessary to identify candidate genes from the human sequence map (J. W. Keele, personal communication).

To supplement this effort with an emphasis on dairy cattle, over 16,500 EST were generated from a cDNA library constructed from eight different stages of mammary gland growth, development, and health. Besides being potential genetic markers for mammary-specific genes, the partially characterized cDNA also serve as a resource for constructing microarrays. These cDNA microarrays can not only be used to better understand the physiology of the mammary gland, but also will be used to enhance identification and evaluation of positional candidate genes by comparing the mRNA expression profiles of animals segregating for different forms of ETL. Genes differentially expressed between phenotypic classes of animals that map within ETL intervals would be considered potential sources of causative variation.

Final Thoughts

The completion of the rough draft of the human sequence map signals an imminent change in how livestock research will be conducted. Genome sequence in-

formation provides an intersection point for research disciplines in mapping, gene expression, biochemistry, and comparative biology. Within this context, an integrated genomics research program provides the infrastructure and resources necessary to develop accurate and reliable MAS schemes and to identify the causative genetic variation or genes underlying ETL in dairy cattle. Included within this infrastructure is the need for collaborative teams of scientists that offer the diverse knowledge and expertise necessary to fully exploit genomics. The depth of future investigations into important dairy traits and the relative ease in which these results are made applicable to industry will be dependent upon the continued development of genomic resources for cattle.

Implications

Marker-assisted selection will have a positive effect on the dairy industry, especially when used to select for traits like dairy form that improve animal health without adversely affecting milk production. Complementing selection with markers should greatly improve the current selection of seedstock while reducing the costs of generating progeny test data. In the future, breed associations and individual producers that implement a comprehensive approach to selection will not only be able to improve production, but also animal health, reproduction and well-being in an intensive production setting.

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